NCAB
Clinical Investigations Subcommittee
September 14, 2009

Expedited Final Summary

Participants:

Dr. Waun Ki Hong, Subcommittee Chair, NCAB
Dr. Lloyd Everson, NCAB
Ms. Kathryn Giusti, NCAB
Ms. Mary Lester, NCAB
Dr. Bruce Chabner, NCAB
Dr. Donald Coffey, NCAB
Dr. Carolyn Runowicz, NCAB
Dr. James Zwiebel, NCI
Dr. Roy Wu, NCI
Dr. Tracy Lively, NCI
Ms. Claire Harris, NCI
Nanci Hemberger (Writer, Scientific Consulting Group, Inc.)

Dr. Hong welcomed participants and introduced the speakers. Dr. Zwiebel presented an overview of the CTEP program for Dr. Jeffrey Abrams, who was unable to attend the meeting. Dr. Wu offered an overview of CTEP's Clinical Grants and Contracts Branch. Dr. Zwiebel also presented a summary of CTEP's Early Clinical Trials Program. Subcommittee comments and questions regarding these presentations and other topics are highlighted below.

CTEP

CTEP highlights include:

- Currently sponsors over 110 INDs
- Includes approximately 11,000 registered investigators at over 3,300 institutions
- Includes more than 1000 active protocols with 500 new protocols/year
- Approximately 30,000 patients accrued/year
- Includes collaborative agreements with more than 80 pharmaceutical companies; provides proprietary data to collaborators

Dr. Chabner noted that while CTEP has expedited therapeutics development it did not initiate the drug investigations.

Dr. Hong asked how the collaborative process is initiated. Dr. Zwiebel said that usually a drug company contacts the person at CTEP responsible for the drug portfolio.

Dr. Chabner asked about the clinical success of particular CTEP clinical trials. Dr. Zwiebel replied that the trials are ongoing so result data are sparse.

Dr. Everson asked if accrual rates to cooperative group trials had decreased over the past 18-24 months. Dr. Zwiebel responded that accrual rates fluctuate regularly but have not dropped off noticeably in recent months. Dr. Everson commented that accrual rates are affected by multiple factors, which must be addressed to encourage and sustain accrual rates in NCI- and academic-supported trials.

A discussion ensued about the importance of biomarkers especially related to new data regarding mutations. One challenge is to identify relevant biomarkers for cancer screening in all patients and for identifying mutation-positive patients.

Large randomized trials for patients who have mutations may not be helpful because these patients may be placed into control groups during the randomization process. Such trials may create hardships for patients with mutations by delaying effective and successful treatment.

CGCB

Dr. Wu discussed CGCB, which manages three grant programs: clinical oncology, surgical oncology, and cancer nutrition as well as serving the administrative and fiscal management of CTEP's extramural research and support contracts.

Dr. Everson asked whether grants are ever ended prematurely. Dr. Wu responded that if accrual rates are low and do not meet target numbers, they are shut down, and the grants are ended. He noted that obtaining data from investigators to support ending a grant can be complicated and take time. Participants discussed the difficulty in ending a trial prematurely even when goals are not being met, and noted the need for stringent criteria that must be enforced. Ms. Lester commented that grants should continue only when target numbers and milestones are met regularly. Dr. Everson agreed but noted that even with such criteria ending trials ahead of schedule remains difficult.

Dr. Hong asked how many R21 grants typically develop into R01s. Dr. Wu replied that he did not have the exact figure but the number was small. Dr. Chabner asked if any significant oncology advances had resulted in the last 5 years from the R21 mechanism; Dr. Wu said not to his knowledge but noted that the P01 portfolio yields the most significant results. Dr. Chabner added that the R21s fund interesting ideas and good researchers and therefore remain valuable.

CTEP's Early Clinical Trials Program

Dr. Zwiebel presented a summary of CTEP's Early Clinical Trials Program, which includes 25 NCI cancer centers. He focused on nine Phase 2 N01s, which are distributed in the United States, Canada, and the Pacific Rim.

Currently the Phase 2 N01 program includes:

- 4560 patients enrolled and 44 agents studied in 215 trials
- 236 LOIs submitted; 56 approved (24%)
- 104 protocols activated
- 81 protocols closed

- 38 investigational combination trials with CTEP-held INDs for both agents
- 18 cancer indications, including rare diseases not likely to be evaluated in company-sponsored trials

The program also plans to coordinate and integrate a tissue acquisition and analysis program with the Cancer Human Biobank and other NCI programs that will facilitate exploration of biomarkers. In addition, PADIS (Pharmacodynamic Assay Development and Implementation Section) develops and validates biomarker assays. Dr. Chabner asked if the assays will be available to the public; Dr. Zwiebel said that the data will not be proprietary, and a goal of the program is to make the assays available to the public.

Dr. Zwiebel also discussed NExT, the NCI Experimental Therapeutics Program. The goal of the program is to shorten the drug development cycle by 1-2 years, with approximately 12 companies and institutions participating in the program. Dr. Chabner noted that a rigorous review process is needed. He added that NCI will be competing against a $20B industry and expressed concern that it may not be the best use of NCI funds. Dr. Coffey wondered if it would be more efficient to share drug development data rather than have many individual institutions involved in drug development, which could cause duplication and excess spending.

The Subcommittee suggested that a recommendation be made to discuss the NExT program at an upcoming NCAB meeting.

Dr. Waun Ki Hong
Chair

10/12/09
Date

Dr. Jeffrey Abrams
Executive Secretary

10/7/09
Date